Gates Foundation Influenza Vaccine Program

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Sustainable Influenza Vaccine Production Capacity Stakeholders' Workshop

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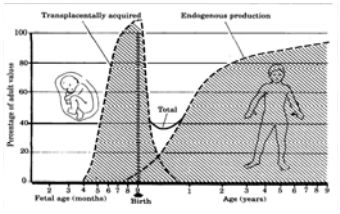
Seasonal and pandemic influenza

- Pandemic efforts initiated in 2004 following re-emergence of H5N1
- Equity is key driver – burden of disease likely to be greater in developing countries due to risk factors/lack of access to tools for prevention and treatment
- Long-term goal for seasonal flu activities is elucidation of impact on/reduction in childhood pneumonia, #1 killer of children
- Projects targeting:
  - » Vaccine probe studies for impact assessment and burden of disease
  - » Data for decision making
  - » New technologies to improve access to seasonal and pandemic influenza vaccines

Mother's Gift Study

Immunizing Mothers Prevents Influenza in Infants

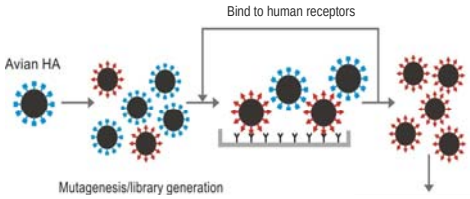


Flu vaccine reduces the rates of respiratory illness with fever

Infants - 34% reduction
Mothers - 63% reduction

Zaman et al. NEJM 2008 Oct 9;359(15):1555-64

"Pre-surveillance": Screening viral protein libraries for pandemic risk assessment



Sequence DNA
Assess pathogenicity
Antigenic cartography
Antibody reagents

Yoshihiro Kawaoka
University of Wisconsin-Madison

Pandemic flu vaccine supply-demand and stockpile logistics analysis

- Work done under contract through Oliver Wyman consulting, initially through PATH grant and in partnership with WHO
- Engaged international stakeholders to analyze supply-demand for influenza vaccines, and logistics of global influenza vaccine stockpile recommended by WHO Strategic Advisory Group of Experts following WHA resolution
- Outputs highlighted need for rapid response/scalable technologies given uncertainties associated with influenza pandemics, confirmed by recent (A)H1N1 outbreak

New technologies promise to reshape the vaccine landscape

Current vaccines

Inactivated, egg based vaccines
- Moderately immunogenic
- Requires injections
- Annual dosing; one year protection

Live attenuated vaccines
- Faster and cheaper to produce
- Can be delivered without syringe
- Potential for improved immunogenicity

Adjuvanted vaccines
- Some cross-protection via robust multi-strain immune response
- Lower cost due to smaller dosage required

New technologies: 5-15 years away

Cross-protective vaccines
- Epitopes and common proteins
- Multi-year utility due multi-strain coverage
- Lower cost, rapidly scalable

Recombinant protein production
- Multiple substrates; e.g.: cell and plant-based
- Lower cost, rapidly scalable
- Longer time required to develop *de novo*

A cross-protective, scalable & affordable vaccine could solve the supply challenges for pandemic influenza preparedness

Influenza vaccine development grants

- PATH Vaccine Solutions Influenza Vaccine Program (IVP)
  - » IEM (live-attenuated)
  - » Lentigen (lentiviral VLPs)
  - » Neugenesis (fungal VLPs)
- University of Texas Medical Branch/VaxInnate
  (*E. coli* produced M2e-flagellin fusion protein)
- Fraunhofer Center for Molecular Biotechnology
  (Transient plant-based production technology)

Technologies of highest interest*

- Live-attenuated vaccines
- Recombinant approaches
- Adjuvants
- Broadly reactive antigens

*Influenza vaccine strategies for broad global access. PATH/Oliver Wyman: www.path.org.

Strategic focus

- Innovation
- Real-time response
- Economics and scalability of vaccine manufacture
- Practical for developing countries
- Viable business model

Summary of Gates Foundation funded influenza program

- Etiology study to determine causes of childhood pneumonia following Hib/pneumococcal vaccine introduction (including influenza)
- Vaccine probe studies to highlight influenza burden and potential health impact of maternal immunization
- Research to improve risk assessment of influenza variants with pandemic potential in advance of human-to-human transmission
- Supply-demand and stockpile logistics analysis to contribute data for global pandemic preparedness decision making
- Investments in new technologies for rapid and inexpensive production of influenza vaccines (including cross-protective approaches)